

CLAIMS

I/WE CLAIM:

1. A method of diagnosis of a transmissible spongiform encephalopathy (TSE) or the possibility thereof in a subject suspected of suffering from the TSE, which comprises subjecting a sample of body fluid taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and has a molecular weight in the range of from 1000 to 100000; and determining whether the test amount is consistent with a diagnosis of TSE.
2. A method according to Claim 1, in which the polypeptide is present in the body fluid of TSE-infected subjects and not present in the body fluid of non-TSE-infected subjects, whereby the presence of the polypeptide in a body fluid sample is indicative of TSE.
3. A method according to Claim 1, in which the polypeptide is not present in the body fluid of TSE-infected subjects and present in the body fluid of non-TSE-infected subjects, whereby the non-presence of the polypeptide in a body fluid sample is indicative of TSE.
4. A method according to Claim 1, in which the mass spectrometry is laser desorption/ionization mass spectrometry.
5. A method according to Claim 4, in which the sample is adsorbed on a probe or on a protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic or weak cationic exchange surface capable of binding the polypeptide.
6. A method according to Claim 4, in which the polypeptide is determined by surface-enhanced laser desorption/ionization (SELDI) and time of flight mass spectrometry (TOF-MS).
7. A method according to Claim 1, in which the body fluid is cerebrospinal fluid, plasma, serum, blood, tears, urine or saliva.
8. A method according to Claim 1, in which a plurality of peptides is determined in the sample.

9. A method according to Claim 1, in which the TSE is Creutzfeldt-Jakob disease (CJD).

10. A method according to Claim 9, in which the TSE is sporadic Creutzfeldt-Jakob Disease (CJD) or variant Creutzfeldt-Jakob Disease (CJD).

11. A method according to Claim 9, in which one or more polypeptides having a respective molecular weight of about 4780, about 6700, about 8600 or about 13375 is determined, and the presence of one or more of such polypeptides is indicative of CJD.

12. A method according to Claim 9 in which one or more polypeptides having a respective molecular weight of about 3970, about 3990, about 4294, about 4478, about 10075, about 11730, about 14043 or about 17839 is determined, and the absence of one or more of such polypeptides is indicative of CJD.

13. A method according to Claim 9, in which a polypeptide having a molecular weight of about 7770 is determined, and the presence of such polypeptide is indicative of CJD.

14. A method according to Claim 9, in which a polypeptide having a molecular weight of about 3295, about 4315, about 4436, about 6200, about 8936, about 9107, about 9145, about 9185, about 9454 or about 13550 Da is determined, and the absence or decreased amount of one or more of such polypeptides is indicative of CJD.

15. A method according to Claim 9, in which a polypeptide having a molecular weight of about 7574, about 7930, about 7975 or about 8020 Da is determined, and the presence or increased amount of one or more of such polypeptides is indicative of CID.

16. A method according to Claim 1, in which the TSE is Bovine Spongiform Encephalopathy (BSE).

17. A method according to Claim 16, in which the polypeptide has a molecular weight of about 10220, and the presence of the polypeptide is indicative of BSE.

18. A method according to Claim 16, in which one or more polypeptides having a respective molecular weight of about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and

31800 Da is determined, and the differential expression of one or more of such polypeptides is indicative of BSE.

19. A method according to Claim 1, in which the TSE is scrapie.
20. A method of diagnosis, prognosis or therapy which comprises use of a polypeptide which is differentially contained in a body fluid of TSE-infected subjects and non-infected subjects, the polypeptide having a molecular weight in the range of from 1000 to 100000 and being determinable by mass spectrometry.
21. A method of diagnosis, prognosis or therapy which comprises use of a material which recognizes, binds to or has affinity for a polypeptide which is differentially contained in a body fluid of TSE-infected subjects and non-infected subjects, the polypeptide having a molecular weight in the range of from 1000 to 100000 and being determinable by mass spectrometry.
22. A method according to Claim 21, in which the material is an antibody or antibody chip.
23. An assay device for use in the diagnosis of TSE which comprises a plate having a location containing a material which recognizes, binds to or has affinity for a polypeptide which is differentially contained in a body fluid of TSE-infected subjects and non-infected subjects, the polypeptide having a molecular weight in the range of from 1000 to 100000 and being determinable by mass spectrometry.
24. An assay device for use in the diagnosis of TSE, which comprises a plate having a location containing an antibody that is specific for Cystatin C.
25. An assay device for use in the diagnosis of variant CJD, which comprises a plate having a location containing an antibody that is specific for Cystatin C and useful in the diagnosis of variant CJD.
26. An assay device for use in the diagnosis of sporadic CJD, which comprises a plate having a location containing an antibody that is specific for Cystatin C and useful in the diagnosis of sporadic CJD.

27. An assay device for use in the diagnosis of BSE, which comprises a plate having a location containing an antibody that is specific for a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof having an immunological reaction to antibodies specific for bovine hemoglobin and useful in the diagnosis of BSE.

28. An assay device for use in the diagnosis of a TSE comprising a solid substrate having attached thereto an antibody that is specific for any of the following:

(i) a polypeptide that is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and has a molecular weight in the range of from 1000 to 100000;

(ii) a polypeptide that is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and is selected from those having a respective molecular weight of about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da

(iii) cystatin C;

(iv) a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin and is differentially contained in the body tissue of bovine TSE-infected subjects and non-bovine non-TSE-infected subjects.

29. A kit for use in diagnosis of TSE, comprising a probe for receiving a sample of body fluid, and for placement in a mass spectrometer, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and has a molecular weight in the range of from 1000 to 100000.

30. A kit according to Claim 29, in which the probe contains an adsorbent for adsorption of the polypeptide.

31. A kit according to Claim 29, further comprising a washing solution for removal of unbound or weakly bound materials from the probe.

32. A method of diagnosis of a transmissible spongiform encephalopathy (TSE) or the possibility thereof in a subject suspected of suffering from the TSE, which comprises determining a test amount of a polypeptide in a sample of body fluid taken from the subject, wherein the polypeptide is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and is Cystatin C; and determining whether the test amount is consistent with a diagnosis of TSE.

33. A method of diagnosis of a transmissible spongiform encephalopathy (TSE) or the possibility thereof in a subject suspected of suffering from the TSE, which comprises subjecting a sample of body fluid taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and is Cystatin C; and determining whether the test amount is consistent with a diagnosis of TSE.

34. The method of claim 33, wherein the body fluid is CSF.

35. A method of diagnosis of a transmissible spongiform encephalopathy (TSE) or the possibility thereof in a bovine subject suspected of suffering from the TSE, which comprises determining a test amount of a polypeptide in a sample of body fluid taken from the subject, wherein the polypeptide is differentially contained in the body fluid of TSE-infected bovine subjects and non-TSE-infected subjects, and is a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin; and determining whether the test amount is consistent with a diagnosis of TSE.

36. A method of diagnosis of a transmissible spongiform encephalopathy (TSE) or the possibility thereof in a bovine subject suspected of suffering from the TSE, which comprises subjecting a sample of body fluid taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of TSE-infected bovine subjects and non-TSE-infected subjects, and is a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin; and determining whether the test amount is consistent with a diagnosis of TSE.

37. A method of providing an indication of a transmissible spongiform encephalopathy (TSE) or the possibility or progress thereof in a subject liable to suffer from the TSE, which comprises use as a marker of a level of at least one polypeptide that has a molecular weight in the range of from 1000 to 100000, is measurable or detectable in the body tissue by mass spectrometry and is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects.

38. The method of claim 37, wherein said at least one polypeptide is selected from those having a respective molecular weight of about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da.

39. The method of claim 37, in which the body fluid is cerebrospinal fluid, plasma, serum, blood, tears, urine or saliva.

40. A method of providing an indication of a transmissible spongiform encephalopathy (TSE) or the possibility or progress thereof in a subject liable to suffer from the TSE, which comprises use as a marker of a level of cystatin C measurable or detectable in a sample of body tissue by mass spectroscopy and differentially contained in the body tissue of TSE-infected subjects and non-TSE-infected subjects.

41. The method of claim 40, wherein the body tissue is from a human subject.

42. The method of claim 40, wherein the body tissue is cerebrospinal fluid.

43. A method of providing an indication of a transmissible spongiform encephalopathy (TSE) or the possibility or progress thereof in a bovine subject liable to suffer from the TSE, which comprises use as a marker of a level of a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin, said level being measurable or detectable in a sample of body tissue by mass spectroscopy, and said hemoglobin, hemoglobin chain or truncated chain or fragment thereof being differentially contained in the body tissue of bovine TSE-infected subjects and non-bovine non-TSE-infected subjects.

44. The method of claim 43, wherein said hemoglobin, hemoglobin chain or truncated chain or fragment thereof has a molecular weight determinable by mass spectroscopy of about 15000 Da, 7500 Da or 3000 Da.

45. The method of claim 43, wherein the sample of body tissue is plasma.

46. The method of claim 43, wherein the sample of body tissue is from a living animal.

47. A bovine animal, or herd of said animals, that has or have been subjected to a test as defined in claim 43 and found to be free of a transmissible spongiform encephalopathy (TSE).